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Claims

1.   An isolated MAGE-A12 HLA class I-binding peptide comprising the amino acid sequence of SEQ ID NO:6, or a functional variant thereof which binds HLA class I molecules comprising one or more amino acid additions, substitutions or deletions.

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2.   The isolated MAGE-A12 HLA class I-binding peptide of claim 1 wherein the isolated peptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:5, fragments thereof, and functional variants thereof.

10   3.   The isolated MAGE-A12 HLA class I-binding peptide of claim 1 wherein the isolated peptide consists of an amino acid sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, fragments thereof, and functional variants thereof.

4.   An isolated MAGE-A12 HLA class I binding peptide comprising a fragment of the
15   amino acid sequence of SEQ ID NO:2 which binds HLA Cw*07, or a functional variant thereof comprising one or more amino acid additions, substitutions or deletions, wherein the functional variant binds HLA Cw*07.

5.   The isolated MAGE-A12 HLA class I-binding peptide of claim 1 or claim 4 wherein
20   the isolated peptide is non-hydrolyzable.

6.   The isolated MAGE-A12 HLA class I-binding peptide of claim 5 wherein the isolated peptide is selected from the group consisting of peptides comprising D-amino acids, peptides comprising a -psi[CH_2NH]-reduced amide peptide bond, peptides comprising a
25   -psi[$COCH_2$]-ketomethylene peptide bond, peptides comprising a -psi[CH(CN)NH]-(cyanomethylene)amino peptide bond, peptides comprising a -psi[$CH_2CH(OH)$]-hydroxyethylene peptide bond, peptides comprising a -psi[CH_2O]-peptide bond, and peptides comprising a -psi[CH_2S]-thiomethylene peptide bond.

30   7.   A composition comprising the isolated MAGE-A12 HLA class I-binding peptide of claim 1 and an isolated HLA class I- or class II-binding peptide of a non-MAGE-A12 tumor antigen.

8.   A composition comprising the isolated MAGE-A12 HLA class I binding peptide of claim 4 and an isolated HLA class I- or class II-binding peptide of a non-MAGE-A12 tumor antigen.

9.   The composition of claim 7 or claim 8, wherein the MAGE-A12 HLA class I-binding peptide and the HLA class I-or class II-binding peptide of a non-MAGE-A12 tumor antigen are combined as a polytope polypeptide.

10.   An isolated nucleic acid encoding a peptide selected from the group consisting of the peptide of any of claims 1-4, wherein the nucleic acid does not encode full length MAGE-A12.

11.   The isolated nucleic acid of claim 10, wherein the nucleic acid comprises a fragment of the nucleotide sequence of SEQ ID NO:1.

12.   An expression vector comprising the isolated nucleic acid of claim 11 operably linked to a promoter.

13.   The expression vector of claim 12 further comprising a nucleic acid which encodes an HLA-Cw*07 molecule.

14.   A host cell transfected or transformed with an expression vector selected from the group consisting of the expression vector of claim 12 and the expression vector of claim 13.

15.   A host cell transfected or transformed with the expression vector of claim 12, wherein the host cell expresses an HLA-Cw*07 molecule.

16.   A method for enriching selectively a population of T lymphocytes with T lymphocytes specific for a MAGE-A12 HLA binding peptide comprising:
        contacting a source of T lymphocytes which contains a population of T lymphocytes with an agent presenting a complex of the MAGE-A12 HLA binding peptide and an HLA

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molecule in an amount sufficient to selectively enrich the population of T lymphocytes with the T lymphocytes specific for a MAGE-A12 HLA binding peptide.

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17.   The method of claim 16, wherein the agent is an antigen presenting cell contacted

5   with a MAGE-A12 protein or an HLA binding fragment thereof.

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18.   The method of claim 16 wherein the MAGE-A12 HLA binding peptide is selected from the group consisting of (i) peptides which consist of a fragment of the amino acid sequence of SEQ ID NO:2, (ii) peptides which comprise the amino acid sequence of SEQ ID

10   NO:6, and (iii) functional variants of the peptides of (i) and (ii).

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19.   A method for diagnosing a disorder characterized by expression of MAGE-A12 comprising:

        contacting a biological sample isolated from a subject with an agent that is specific for

15   a MAGE-A12 HLA binding peptide, and

        determining the interaction between the agent and the MAGE-A12 HLA binding peptide as a determination of the disorder.

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20.   The method of claim 19 wherein the MAGE-A12 HLA binding peptide is selected

20   from the group consisting of (i) peptides which consist of a fragment of the amino acid sequence of SEQ ID NO:2, (ii) peptides which comprise the amino acid sequence of SEQ ID NO:6, and (iii) functional variants of the peptides of (i) and (ii).

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21.   A method for diagnosing a disorder characterized by expression of a MAGE-A12

25   HLA binding peptide, comprising:

        contacting a biological sample isolated from a subject with an agent that binds the complex; and

        determining binding between the complex and the agent as a determination of the disorder.

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22.   The method of claim 21 wherein the MAGE-A12 HLA binding peptide is selected from the group consisting (i) peptides which consist of a fragment of the amino acid sequence

of SEQ ID NO:2, (ii) peptides which comprise the amino acid sequence of SEQ ID NO:6, and (iii) functional variants of the peptides of (i) and (ii).

23. A method for treating a subject having a disorder characterized by expression of MAGE-A12, comprising:

administering to the subject an amount of a MAGE-A12 HLA binding peptide sufficient to ameliorate the disorder.

24. The method of claim 23, wherein the MAGE-A12 HLA binding peptide is selected from the group consisting of (i) peptides which consist of a fragment of the amino acid sequence of SEQ ID NO:2, (ii) peptides which comprise the amino acid sequence of SEQ ID NO:6, and (iii) functional variants of the peptides of (i) and (ii).

25. A method for treating a subject having a disorder characterized by expression of MAGE-A12, comprising:

administering to the subject an amount of the composition of claim 7 or claim 8 sufficient to ameliorate the disorder.

26. A method for treating a subject having a disorder characterized by expression of MAGE-A12, comprising:

administering to the subject an amount of an agent which enriches selectively in the subject the presence of complexes of an HLA molecule and a MAGE-A12 HLA binding peptide, sufficient to ameliorate the disorder.

27. The method of claim 26, wherein the agent comprises a MAGE-A12 HLA binding peptide.

28. The method of claim 26 or claim 27 wherein the MAGE-A12 HLA binding peptide is selected from the group consisting of (i) peptides which consist of a fragment of the amino acid sequence of SEQ ID NO:2, (ii) peptides which comprise the amino acid sequence of SEQ ID NO:6, and (iii) functional variants of the peptides of (i) and (ii).

29.   A method for treating a subject having a disorder characterized by expression of MAGE-A12, comprising:

        administering to the subject an amount of autologous T lymphocytes sufficient to ameliorate the disorder, wherein the T lymphocytes are specific for complexes of an HLA molecule and a MAGE-A12 HLA binding peptide.

30.   The method of claim 29 wherein the MAGE-A12 HLA binding peptide is selected from the group consisting of (i) peptides which consist of a fragment of the amino acid sequence of SEQ ID NO:2, (ii) peptides which comprise the amino acid sequence of SEQ ID NO:6, and (iii) functional variants of the peptides of (i) and (ii).

31.   A method for identifying functional variants of a MAGE-A12 HLA binding peptide, comprising

        selecting a MAGE-A12 HLA binding peptide, an HLA binding molecule which binds the MAGE-A12 HLA class I binding peptide, and a T cell which is stimulated by the MAGE-A12 HLA binding peptide presented by the HLA binding molecule;

        mutating a first amino acid residue of the MAGE-A12 HLA binding peptide to prepare a variant peptide; and

        determining the binding of the variant peptide to HLA binding molecule and the stimulation of the T cell, wherein binding of the variant peptide to the HLA binding molecule and stimulation of the T cell by the variant peptide presented by the HLA binding molecule indicates that the variant peptide is a functional variant.

32.   The method of claim 31, wherein the MAGE-A12 HLA binding peptide is selected from the group consisting of (i) peptides which consist of a fragment of the amino acid sequence of SEQ ID NO:2, and (ii) peptides which comprise the amino acid sequence of SEQ ID NO:6.

33.   The method of claim 31, further comprising the step of comparing the stimulation of the T cell by the MAGE-A12 HLA binding peptide and the stimulation of the T cell by the functional variant as a determination of the effectiveness of the stimulation of the T cell by the functional variant.

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Sub A37 34.   An isolated polypeptide which binds selectively a polypeptide of any of claims 1-4, provided that the isolated polypeptide is not an HLA molecule.

5   35.   The isolated polypeptide of claim 34, wherein the isolated polypeptide is an antibody.

36.   The antibody of claim 35, wherein the antibody is a monoclonal antibody.

37.   The isolated polypeptide of claim 34, wherein the isolated polypeptide is an antibody
10   fragment selected from the group consisting of a Fab fragment, a F(ab)$_2$ fragment or a fragment including a CDR3 region selective for a MAGE-A12 HLA binding peptide.

38.   An isolated T lymphocyte which selectively binds a complex of an HLA molecule and a MAGE-A12 HLA binding peptide.

15   39.   The isolated T lymphocyte of claim 38 wherein the MAGE-A12 HLA binding peptide is selected from the group consisting of (i) peptides which consist of a fragment of the amino acid sequence of SEQ ID NO:2, (ii) peptides which comprise the amino acid sequence of SEQ ID NO:6, and (iii) functional variants of the peptides of (i) and (ii).

20   40.   An isolated antigen presenting cell which comprises a complex of an HLA molecule and a MAGE-A12 HLA binding peptide.

41.   The isolated antigen presenting cell of claim 40 wherein the MAGE-A12 HLA
25   binding peptide is selected from the group consisting of (i) peptides which consist of a fragment of the amino acid sequence of SEQ ID NO:2, (ii) peptides which comprise the amino acid sequence of SEQ ID NO:6 and (iii) functional variants of the peptides of (i) and (ii).

Sub A4 42.   A vaccine composition comprising the polypeptide of any of claims 1-4 and a pharmaceutically acceptable carrier.

43.   The vaccine composition of claim 42, further comprising an adjuvant.

Sub A57 44.   A vaccine composition comprising a cell selected from the group consisting of a T

lymphocyte of claims 38 and 39 and an antigen presenting cell of claims 40 and 41, and a

5   pharmaceutically acceptable carrier.

45.   The vaccine composition of claim 44, further comprising an adjuvant.

46.   A vaccine comprising the isolated nucleic acid molecule of claim 10 and a

10   pharmaceutically acceptable carrier.

47.   The vaccine of claim 46, further comprising an adjuvant.

48.   An isolated functional variant of a MAGE-A12 HLA binding peptide identified by the

15   method of claim 31.

49.   A method for identifying a candidate mimetic of a MAGE-A12 HLA binding peptide,

comprising

        providing a HLA molecule which binds the MAGE-A12 HLA binding peptide,

20   contacting the HLA molecule with a test molecule, and

        determining the binding of the test molecule to the HLA molecule, wherein a test

molecule which binds to the HLA molecule is a candidate mimetic of the MAGE-A12 HLA

binding peptide.

25 50.   The method of claim 49, further comprising

        forming a complex of the HLA molecule and the candidate mimetic,

        contacting the complex with a T cell which binds to a complex of an HLA molecule

and the MAGE-A12 HLA binding peptide, and

        assaying activation of the T cell.

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51.   The method of claim 50, wherein activation of the T cell is indicated by a property

selected from the group consisting of proliferation of the T cell, interferon-γ production by the

T cell, tumor necrosis factor production by the T cell, and cytolysis of a target cell by the T cell.

52. A protein microarray comprising an isolated MAGE-A12 HLA class I-binding peptide or a functional variant thereof which binds HLA class I molecules comprising one or more amino acid additions, substitutions or deletions.

53. The protein microarray of claim 52, wherein the isolated MAGE-A12 HLA class I-binding peptide comprises the amino acid sequence of SEQ ID NO:6.

54. The protein microarray of claim 52, wherein isolated MAGE-A12 HLA class I-binding peptide comprises an amino acid sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:5, and functional variants thereof.

55. A method for diagnosing a disorder characterized by expression of MAGE-A12 comprising,

contacting the protein microarray of claim 52 with a biological sample isolated from a subject suspected of having the disorder, and

determining the binding of a constituent of the biological sample to the isolated MAGE-A12 HLA class I binding peptide.

56. The method of claim 55, wherein the constituent of the biological sample is selected from the group consisting of an antibody, a T lymphocyte, and a HLA molecule.

57. The method of claim 55, wherein the disorder is cancer.